3. Claims 1-5 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Essigmann *et al.* in light of Güler *et al.*, "A Cyanobacterial Gene, *sqdX*, Required for Biosynthesis of the Sulfolipid Sulfoquinovosyldiacylglycerol, *J. Bacteriol.*, 182: 543-45 (2000).

4. Claims 1-2 and 4-5 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Essigmann *et al.* in light of Mulichak *et al.*, "Crystal structure of SQD1, an enzyme involved in the biosynthesis of the plant sulfolipid headgroup donor UDP-sulfoquinovose," *Proc. Natl. Acad. Sci. USA*, 96: 13097-13102 (1999).

I. CLAIMS 1-5 ARE SUFFICIENTLY DESCRIBED AND ENABLED BY THE SPECIFICATION AS FILED

A. The Claimed Embodiment is Sufficiently Described

The Examiner rejected Claim 1 (and its dependent Claims 2-5) under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (*See* Office Action Mailed 5/9/01, p. 5). Specifically, the Examiner rejected Claim 1 on the following two grounds:

> a) "the specification fails to describe other representative species [of polypeptides] by any characteristics or structural properties other than the functionality of SQD1 activity and sulfolipid synthase activity;" and
> b) "the specification does not describe the common characteristics of a suitable sulfur donor."

(Office Action Mailed 5/9/01, pp. 4-5).

Applicants believe that the claimed embodiment is supported by a sufficient description as provided in the Specification. As noted in the case *In re Angstadt*, Applicants "are not required to disclose every species encompassed by their claims even in an unpredictable art." *In re Angstadt*, 537 F.2d 498, 502-03 (C.C.P.A. 1976); *See Regents of the Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997). Thus, the peptides contemplated by the claimed embodiment are "described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the

time the application was filed, had possession of the claimed invention" under 35 U.S.C. § 112.

Moreover, with respect to the appropriate sulfur donor to be used in the methods of the claimed embodiment or the "common characteristics of a suitable sulfur donor," the Specification as filed provides five examples of suitable sulfur donors (*e.g.* sulfate, sulfide, thiosulfate, sulfoglutathione, adenosine 5'-phosphosulfate, and 3'-phosphoadenosine-5'-phosphosulfate (PAPS)) and states that *sulfite* is a preferred donor. (*See* p. 3, ll. 16-19, and p. 13, ll. 13-17, of Application Ser. No. 09/709,020 as filed). In light of the holdings in *Angstadt* and *Eli Lilly* noted above, Applicants are not required to provide an exhaustive teaching as to all possible sulfur donors that may be utilized in the methods of the present invention. Thus, the sulfur donors contemplated by the claimed embodiment are "described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" under 35 U.S.C. § 112.

Applicants believe that the Specification as filed provides a sufficient description for the subject matter as claimed. However, without acquiescing to the Examiner's rejection, but to further the prosecution, and hereby expressly reserving the right to prosecute the claims as originally filed (or similar claims), the Applicants have cancelled Claims 2-5, and amended Claim 1 to further define one embodiment of the present invention. Applicants believe that the Claims as amended render the Examiner's rejection moot.

B. The Claimed Embodiment is Sufficiently Enabled

The Examiner also rejected Claims 1, 2-5 under 35 U.S.C. § 112, first paragraph because "[t]he specification as filed does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with [the] claims." (Office Action Mailed 5/9/01, p. 5). Applicants do not argue.

In any event, Applicants believe that, in view of the amendments made above, the rejection is moot. As the Examiner expressly indicates, the Specification is "enabling for a method of producing SQDG using SQD1 of SEQ ID NO: 6 and sulfolipid synthase of SEQ ID NO: 1 and 2-5 and enzymatically active fragments thereof." (Office Action Mailed 5/9/01,

p. 5). Moreover, the Specification provides several examples (Example 4, for instance) of methods which one skilled in the art may use to obtain the peptides of the claimed embodiment. (*See, e.g.*, pp. 50-57 of Application Ser. No. 09/709,020 as filed).

II. CLAIMS 1-2, 5 AND 13-14 ARE NOT ANTICIPATED BY ESSIGMANN *ET AL.*

The Examiner rejected Claims 1-2, 5, 13 and 14 under 35 U.S.C. § 102(b) as being anticipated by Essigmann *et al.* However, the reference cited is invalid as a proper basis for a rejection based on anticipation under § 102(b) because: a) the reference is not enabled; and b) the reference does not teach all of the elements of the claimed embodiment. Therefore, the Examiner's rejection must fall.

A. The Reference is Not Enabled

In order to be considered valid prior art under § 102(b), a reference "must put the anticipating subject matter at issue into the possession of the public through an enabling disclosure." *Chester v. Miller*, 906 F.2d 1574, 15 U.S.P.Q.2d 1333 (Fed. Cir. 1990). Applicants argue that, in the present case, the reference merely offers a starting point for further experiments (*i.e.* an mere invitation to experiment based on a hypothesis or speculation) and does not provide adequate directions for one skilled in the art to practice the invention as dictated by *Dewey & Almy Chem. Co. v. Mimex Co.*, 124 F.2d 986, 989 (2d. Cir. N.Y. 1942). In *Dewey*, the Second Circuit Court of Appeals stated:

> "No doctrine of the patent law is better established than that a prior patent or other publication to be an anticipation must bear within its four corners adequate directions for the practice of the patent invalidated. If the earlier disclosure offers no more than a starting point for further experiments, if its teaching will sometimes succeed and sometimes fail, if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation."

Id.

Specifically, the Examiner asserts that the reference cited teaches "how to make sulfoquinovosyldiacylglycerol (SQDG) using UDP-glucose, a sulfur donor, SQD1, and a *sulfolipid synthase* that catalyzes transfer of the sulfoquinovose to diacylglycerol (page 31, Fig. 1, and page 31, 3rd through 4th paragraph)." (*See* Office Action Mailed May 9, 2001, p.7)(emphasis added). However, at no place in the reference cited does the term "*sulfolipid*

synthase that catalyzes transfer of the sulfoquinovose to diacylglycerol" appear. In fact, Figure 1 of the reference cited provides only a proposed chemical model of the "sugar-nucleotide pathway for sulfolipid biosynthesis." Moreover, although the legend for Figure 1 indicates that "the UDP-sulfoquinovose moiety is transferred to diacylglycerol," it is completely silent as to what transfers the UDP-sulfoquinovose moiety to diacylglycerol.

With respect to the material cited from the reference (page 31, 4th paragraph), the Examiner appears to be referring to the following statement as a basis for indicating that the cited reference teaches a method whereby the UDP-sulfoquinovose moiety is transferred to diacylglycerol:

> "With the demonstration of UDP-sulfoquinovose accumulation in the *R. sphaeroides* null mutant and the characterization of UDP-sulfoquinovose: diacylglycerol sulfoquinovosyltransferase from spinach (17, 18), the last step of SQDG biosynthesis has been clarified."

However, the material cited (and, therefore, the reference as a whole) fails to satisfy the anticipation standard as stated in *Dewey* because the mere mention of such a transferase, without any further teaching in the reference, "does not inform the art ... how to practice the new invention." *Dewey*, 124 F.2d at 989. If anything, the material cited (page 31, 4th paragraph) only points to work done by others (*i.e.* references 17 and 18 of the above reference) and indicates the mere existence of a putative UDP-sulfoquinovose:diacylglycerol sulfoquinovosyl transferase. Therefore, the reference does not *teach* a necessary element of the claimed embodiment (*i.e.* a second peptide capable of transferring sulfoquinovose from UDP-SQ onto diacylglycerol). As such, Essigmann *et al.* does not enable one skilled in the art to practice the claimed embodiment and is insufficient as a basis for an anticipation rejection under § 102(b).

B. The Reference Does Not Teach Each and Every Element

In order for a prior art reference "to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." *In re Bond*, 910 F.2d 831 (Fed. Cir. 1990). Applicants argue that, in the present case, Essigmann *et al.* is an improper basis for a rejection based on anticipation because the reference does not teach every element of the claimed embodiment.

First, with respect to sulfur donors as they relate to the methods of the claimed embodiment of Claims 1 and 13, the Examiner clearly points out that "Essigmann *et al.* do not teach how to make SQDG using various sulfur groups." (Office Action Mailed 5/9/01, p. 9). In fact, Essigmann *et al.* expressly teaches that the identity of the sulfur donor is "currently under investigation," that a "functional assay for SQD1 is not possible due to the unknown identity of the sulfur donor," and merely suggests possible "scenarios" in which sulfite (or another donor) may be involved in the formation of UDP-SQ. (Essigmann *et al.*, pp. 36, 38 & 40). Therefore, the reference cited does not disclose the sulfur donor element of the claimed embodiment.

Moreover, with respect to Claim 13, the specific material cited by the Examiner does not state that "SQD1 converts UDP-glucose to UDP-sulfoquinovose." (Office Action Mailed 5/9/01, p. 7). Rather, the reference merely teaches that prior research has "led to the suggestion that SQD1 is involved in the first step of the biosynthetic pathway, the formation of UDP-sulfoquinovose" and that the enzyme UDP-glucose/galactose epimerase from *E. coli* "catalyzes the interconversion of UDP-glucose and UDP-galactose." (Essigmann *et al.*, p. 31, 4th full paragraph). The reference neither teaches, nor discloses the nucleic acid sequence of, "a peptide capable of transferring sulfoquinovose from uridine 5'-diphosphosulfoquinovose onto diacylglycerol" as expressly stated in Claim 13 as filed. (*See* Claim 13, p. 80, ll. 16-18 of Application Ser. No. 09/709,020 as filed). Thus, the reference cited does not teach each and every element of the claimed embodiment, and Claim 13 is not anticipated. Therefore, for the reasons stated above, Claims 1 and 13 are not anticipated under 35 U.S.C. § 102(b) by Essigmann *et al.*

III. CLAIMS 1-5 ARE PATENTABLE OVER THE REFERENCES CITED

The Examiner has rejected Claims 1-5 under 35 U.S.C. 103(a) as being unpatentable over Essigmann *et al.* in view of Güler *et al.* The Examiner is reminded that a *prima facie* case of obviousness requires citation to a combination of references which (A) suggests or motivates one of skill in the art to combine the elements to yield the claimed combination, (B) provides a reasonable expectation of success should the claimed combination be carried out, and (C) discloses the elements of the claimed embodiment. Failure to establish any one of these three requirements precludes a finding of a *prima facie* case of obviousness, and,

without more, entitles Applicant to allowance of the claims in issue. *See, e.g., Northern Telecom Inc. v. Datapoint Corp.*, 15 U.S.P.Q. 2d 1321, 1323 (Fed. Cir. 1990).

The Applicant respectively submits the Examiner has failed to establish the elements of a *prima facie* case of obviousness. In addressing this rejection, Applicants focus on independent Claim 1 since non-obviousness of an independent claim necessarily leads to non-obviousness of claims dependent therefrom. *MPEP* § 2143.03.

A. There Is No Motivation to Combine the References

A proper analysis, in view of 35 U.S.C. § 103, demands the references cited by the Examiner be considered as a whole and must suggest the desirability and thereby, the obviousness, of making the combination. *Hodash v. Block Drug Co.*, 786 F. 2d 1136, 1143, n.5, 229 U.S.P.Q. 182, 187, n.5 (Fed. Cir. 1986); *MPEP* § 2141. Moreover, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." MPEP § 2141.01 (citing *In re Mills*, 916 F.2d 680, U.S.P.Q.2d 1430 (Fed. Cir. 1990).

The Examiner has failed to indicate, wherein the references cited, there is such a suggestion of desirability to combine. Applicants submit that references cannot be considered collectively until the Examiner points to some motivation to combine said references, rather than a motivation to employ (as the Examiner has indicated), portions of said references. (*See* Office Action Mailed 05/09/01, p. 8). This proper analysis prevents the Examiner from using the instant Specification to reconstruct, in hindsight, the invention as claimed. The Federal Circuit, in a recent decision, articulated the policy behind this analysis:

> "To prevent the use of hindsight based on the invention to defeat patentability of the invention, this court requires the examiner to show a motivation to combine the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed."

In re Rouffet, 149 F.3d 1350, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998).

As noted above, the Examiner admits that "Essigmann *et al.* do not teach how to make SQDG using various sulfur groups." (Office Action Mailed 5/9/01, p. 9). Although Güler *et al.* teaches the use of a peptide encoded by the *sqdX* gene to produce SQDG, the reference

neither teaches, nor suggests, using the peptides of the claimed embodiment and various sulfur groups (*i.e.* donors) in combination to produce SQDG. Therefore, the cited prior art does not suggest the desirability of making the combination of elements set forth in the claims at issue in the present case. Thus, the Examiner cannot point to a basis for combining the references. and the rejection cannot stand.

B. The References Do Not Disclose a Reasonable Expectation of Success

A proper analysis under 35 U.S.C. § 103 requires that a combination of references must provide a reasonable expectation of success should the claimed combination be carried out. *MPEP* § 2143.02. Moreover, "both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442, 947 F.2d 488 (Fed. Cir. 1991). The Examiner has failed to indicate, wherein the references cited, there is any such disclosure. In the same way that the Essigmann *et al.* and Güler *et al.* do not suggest the desirability of making the combination, both references are similarly silent with respect to whether one skilled in the art would have a reasonable expectation of success should the claimed combination be carried out. Since the Examiner has not done this, the rejection cannot stand.

The Examiner has failed to provide a reference or combination of references which reasonably suggests or teaches the limitations of the claims at issue. Therefore the rejection appears to be based on the Examiner's beliefs rather than the prior art. This is improper. Accordingly, the Claim 1, and its dependent Claims 2-5, are not obvious and should be passed to allowance.

C. Even if Combined (Improperly), The References Do Not Teach All of The Elements

Finally, Essigmann *et al.* teaches that the identity of the sulfur donor involved in sulfolipid biosynthesis is unknown (*see* Essigmann *et al.*, p. 36, Col. 2, 1st paragraph and Mulichak *et al.*, p. 13097, abstract). Although Güler *et al.* teaches the use of a peptide encoded by the *sqdX* gene to produce SQDG, the reference neither teaches, nor suggests, using the peptides of the claimed embodiment and various sulfur groups (*e.g.* sulfite) in combination to produce SQDG. Thus, even if said references were to be improperly

combined, they still would not teach the production of UDP-sulfoquinovose, and its subsequent modification to SQDG, by a method using sulfite, uridine-5'-diphosphoglucose, and said recombinant peptides. Therefore, the elements of the claimed embodiment is not taught as is required in a proper analysis under 35 U.S.C. § 103. *MPEP* § 2143.03.

IV. CLAIMS 1-2 AND 4-5 ARE PATENTABLE OVER THE REFERENCES CITED

The Examiner has rejected Claims 1-2 and 4-5 under 35 U.S.C. 103(a) as being unpatentable over Essigmann *et al.* in view of Mulichak *et al.* The Applicant respectively submits the Examiner has failed to establish the elements of a *prima facie* case of obviousness. In addressing this rejection, Applicants focus on independent Claim 1 since non-obviousness of an independent claim necessarily leads to non-obviousness of claims dependent therefrom. *MPEP* § 2143.03.

A. There Is No Motivation to Combine the References

A proper analysis, in view of 35 U.S.C. § 103, demands the references cited by the Examiner be considered as a whole and must suggest the desirability and thereby, the obviousness, of making the combination. *Hodash*, 786 F. 2d at 1143, n.5, 229 U.S.P.Q. at 187, n.5 (Fed. Cir. 1986); *MPEP* § 2141. The Examiner has failed to indicate, wherein the references cited, there is such a suggestion of desirability to combine.

Specifically, as noted above, Essigmann et al. does not *teach* a necessary element of the claimed embodiment (*i.e.* a second peptide capable of transferring sulfoquinovose from UDP-SQ onto diacylglycerol). Although Mulichak *et al.* suggests possible sulfur donors to produce UDP-sulfoquinovose (*see, e.g.*, Mulichak *et al.*, p. 13101, Col. 1, 1st paragraph), the reference neither teaches, nor suggests, using the peptides of the claimed embodiment in combination with various sulfur donors to produce SQDG. Moreover, both Essigmann *et al.* and Mulichak *et al.* (as admitted by the Examiner) teach that the identity of the sulfur donor involved in sulfolipid biosynthesis is unknown (*see* Essigmann *et al.*, p. 36, Col. 2, 1st paragraph and Mulichak *et al.*, p. 13097, abstract), the reference neither teaches, nor suggests, using the various sulfur donors disclosed by Mulichak *et al.* (or by the Specification of the present invention).

Therefore, the cited prior art does not suggest the desirability of making the combination of elements set forth in the claims at issue in the present case. Thus, the Examiner cannot point to a basis for combining the references and the rejection cannot stand.

B. The References Do Not Disclose a Reasonable Expectation of Success

A proper analysis under 35 U.S.C. § 103 requires that a combination of references must provide a reasonable expectation of success should the claimed combination be carried out. MPEP § 2143.02. Moreover, "both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442, 947 F.2d 488 (Fed. Cir. 1991). Essigmann *et al.* and Mulichak *et al.* do not suggest the desirability of making the combination; both references are silent with respect to whether one skilled in the art would have a reasonable expectation of success should the claimed combination be carried out.

For example, as the Examiner has repeatedly pointed out, Mulichak *et al.* teaches that the sulfur donor involved in the biosynthesis of SQDG is unknown. (*See* Office Action mailed 05/09/01, pp. 5 & 9). Mulichak *et al.* does not teach a preferred donor or which donor is likely to result in the *successful* production of SQDG. Moreover, the Examiner has failed to indicate, wherein the references cited, there is any disclosure as to a reasonable expectation of success if one skilled in the art were to combine the two references in order to practice the claimed embodiment. Therefore, the Examiner's rejection based on 35 U.S.C. § 103 must fall.

C. Even If Combined (Improperly), The References Do Not Teach All of The Elements

One embodiment of the claimed embodiment teaches the production of UDP-sulfoquinovose, and its subsequent modification to SQDG, by a method using sulfite, uridine-5'-diphosphoglucose, a first peptide capable of catalyzing the conversion of UDP-diphosphoglucose to UDP-SQ and a second capable of transferring sulfoquinovose from UDP-SQ onto diacylglycerol. (*See* Claim 1, p. 80 of Application Ser. No. 09/709,020 as filed). As indicated above, Essigmann *et al.* does not teach a method of producing SQDG using said peptides (*i.e.* specifically, said second peptide). Thus, even if the references were improperly

combined, each and every element of the claimed embodiment would not be disclosed. Therefore, the claimed embodiment is not taught as is required in a proper analysis under 35 U.S.C. § 103. *MPEP* § 2143.03.

Moreover, the Specification as filed notes that "[u]nlike the current methods for the synthesis of UDP-SQ,"[2] the synthesis methods of the claimed embodiment are "rapid" and that "the production of UDP-SQ by the methods of the present invention can be completed in less than an hour." (*See* p. 3, ll. 1-5, of Application Ser. No. 09/709,020 as filed). These advantages of the claimed embodiment are primarily due to the fact that the claimed embodiment involves recombinant "first and second" peptides for the biosynthesis of UDP-SQ and its subsequent modification to SQDG. Neither Essigmann *et al.*, nor Mulichak *et al.*, teach or suggest such an approach or the resulting advantages.

CONCLUSION

The Applicant believes that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that these grounds for rejection be withdrawn for the reasons set above. Applicants have added Claims 15 and 16 to further clarify one embodiment of the present invention. Moreover, Applicants believe that said claims are consistent with the provisional election made in response to the Examiner's Restriction Requirement referred to herein. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants' encourage the Examiner to call the undersigned collect at 617.252.3353.

Dated: October 5, 2001

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[2] For a discussion of prior art methods for the synthesis of UDP-SQ, *see* p. 2, ll. 12-24 of Application Ser. No. 09/709,020 as filed and the references cited therein.

APPENDIX I
MARKED-UP VERSION OF REWRITTEN CLAIMS

The following is a version of the claims pursuant to 37 C.F.R. § 1.121(c)(1)(ii) with markings showing the changes made herein to the previous version of record of the claims.

1.(Amended) A method, comprising:

a) providing:

i) uridine-5'-diphosphoglucose;

ii) sulfite [a sulfur donor];

iii) a first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6[capable of catalyzing the conversion of uridine-5'-diphosphoglucose to uridine-5'-diphosphosulfoquinovose]; and

iv) a second peptide encoded by a nucleic acid selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3[capable of transferring sulfoquinovose from uridine-5'-diphosphosulfoquinovose onto diacylglycerol];

b) reacting said uridine-5'-diphosphoglucose with said first peptide and said sulfite [sulfur donor] under such conditions that uridine-5'-diphosphosulfoquinovose is generated; and

c) treating said uridine-5'-diphosphosulfoquinovose with said second peptide under conditions such that sulfoquinovose diacylglycerol is generated.

13.(Amended) A method, comprising:

a) providing:

i) uridine-5'-diphosphoglucose;

ii) sulfite [a sulfur donor]; and

iii) a peptide encoded by the nucleic acid sequence set forth in SEQ ID NO:[5] 6; and

b) reacting said uridine-5'-diphosphoglucose with said peptide and said sulfite [sulfur donor] under such conditions that uridine-5'-diphosphosulfoquinovose is generated.